CADTH

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Vital Pulp Therapy for Endodontic Treatment of Mature Teeth: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	July 10, 2019
Report Length:	31 Pages

CADTH

Authors: Charlotte Wells, Camille Dulong, Suzanne McCormack

Cite As: Vital pulp therapy for endodontic treatment of mature teeth: a review of clinical effectiveness, cost-effectiveness, and guidelines. Ottawa: CADTH; 2019 Jul. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to Requests@CADTH.ca

Abbreviations

CaOH	calcium hydroxide
CEM	calcium enriched mixture
MTA	mineral trioxide aggregate
PAI	periapical index
PRF	platelet rich fibrin
RC	root canal
RCT	randomized controlled trial
SR	systematic review
VAS	visual analogue scale
VPT	vital pulp therapy
ZOE	zinc oxide and/with eugenol

Context and Policy Issues

Dental pulp is a type of connective tissue found within the hard tissues (dentine and enamel) of the teeth.[1] When exposed to damage such as caries or tooth fracture, dental pulp is at risk of infection, which can lead to pain, necrosis, and infection of the jaw bone and surrounding tissues.[1] Currently in permanent teeth (secondary dentition), root canal (usually compromised of a pulpectomy [removal of the vital pulp in the tooth], refilling with synthetic material, and sealing), is the most common treatment for infected pulp.

Vital pulp therapy (VPT) is a potential alternative to root canal treatment (RC).[2] VPT is a restorative dental procedure that aims to treat teeth with compromised dental pulp without the full removal or excavation of all healthy pulp tissue.[2] It is commonly performed in primary dentition (also known as baby teeth), as primary dentition has not fully developed the apical root, but is less commonly performed in secondary dentition. VPT can include indirect or direct pulp capping (i.e., placement of a protective material over the pulp) and partial or full pulpotomy (i.e., removal of part or all of the coronal pulp). Dressings used in VPT can include resin modified glass ionomers, adhesive resins, calcium hydroxide (CaOH), mineral trioxide aggregate (MTA), and bioceramics.[2]

VPT may be of benefit to patients with secondary dentition as it may help prolong survival of the tooth, especially molar teeth.[2] As the forces exerted on teeth during mastication (i.e., chewing) are very high, endodontically-treated teeth with RC can be at risk of structural failure. Teeth treated with RC are also at risk of loss of sensation of environmental changes (potentially leading to more or worse caries), rejection of the foreign material, reinfection, and occurrence of apical periodontitis.[1,2]

Success of VPT is dependent on a variety of factors, including the amount of infected tissue, an adequate blood supply to the tooth, healthy periodontium, and the opportunity to create an appropriate coronal seal.[2] VPT is of interest to dentists as an alternative to RC,

as the ability to restore or salvage vital pulp can be beneficial to patients, despite the generally successful results with RC treatment.[1]

The purpose of this report is to evaluate the clinical evidence regarding the clinical effectiveness and safety of vital pulp therapies compared with RC, and to evaluate available cost-effectiveness data to support reimbursement decision making. Additionally, evidence-based recommendations were sought to provide guidance on the use of VPT in secondary dentition.

Research Questions

1. What is the clinical effectiveness of vital pulp therapy on mature teeth?
2. What is the cost-effectiveness of vital pulp therapy on mature teeth?
3. What are the evidence-based guidelines for vital pulp therapy on mature teeth?

Key Findings

Evidence from one very low-quality systematic review, and four very low to moderate-quality primary studies suggest that clinical success rates for teeth treated with vital pulp therapy or pulpotomy may not significantly differ from teeth treated with root canal therapy or pulpectomy. Findings were comparable between vital pulp therapy and root canal or in favour of vital pulp therapy for short-term (one week) post-operative pain reduction.

One well-conducted economic evaluation from Germany found that direct pulp capping was cost-effective when compared with root canal in most cases, including when the willingness-to-pay ceiling value was adjusted (from 0 to 250 euro). Sensitivity analyses found direct pulp capping was not cost-effective in patients over 40 years of age or with teeth with a proximal pulp exposure.

No guidelines regarding vital pulp therapies with any materials were identified.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were pulpotomy or vital pulp therapy and mature teeth or adults. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2014 and June 10, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1-3: Adults requiring endodontic, pulpal or periapical treatments on any mature teeth
Intervention	Q1-3: Vital pulp therapy (i.e., indirect pulp capping, direct pulp capping, partial pulpotomy, and full pulpotomy)
Comparator	Q1,2: Root canal therapy (i.e., pulpectomy) Q3: Not applicable
Outcomes	Q1: Effectiveness (e.g., symptoms, dental fitness, clinical stability, radiographic stability, periradicular radiolucencies, periradicular healing, duration until treatment failure); Safety (e.g., side effects, adverse events, tooth weakening, susceptibility to caries, susceptibility to fracture due to a loss of the proprioceptive mechanism, susceptibility to fracture in general, tooth loss) Q2: Cost-effectiveness (e.g., incremental cost per health benefit gained, quality adjusted life years, cost per patient adverse event avoided, cost per clinical outcome) Q3: Guidelines on appropriate use and its place in therapy
Study Designs	Health technology assessments, systematic reviews, meta-analyses, non-randomized studies, economic evaluations, evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Guidelines with unclear methodology and studies that did not report comparative results between root canal therapy and vital pulp therapy were also excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using Assessing the Methodological Quality of Systematic Reviews (AMSTAR) 2,[3] randomized and non-randomized studies were critically appraised using the Down's and Black Checklist,[4] and economic studies were assessed using the Drummond checklist.[5] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 536 citations were identified in the literature search. Following screening of titles and abstracts, 513 citations were excluded and 23 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 18 publications were excluded for various reasons, and six publications met the inclusion criteria and were included in this report. These comprised one systematic review (SR),[6] three randomized controlled trials (RCTs),[7-9] one non-randomized study,[10] and one economic evaluation.[11] No evidence-based guidelines were identified regarding VPT for mature permanent teeth. Appendix 1 presents the PRISMA[12] flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Systematic Review

The included SR[6] was published in 2018. The authors included nine studies within the report, with four of these studies providing relevant results for the present report. The nine included studies were a variety of designs, including RCTs, clinical trials, and case studies, but the four relevant studies were labeled by the authors as clinical trials and RCTs. The remaining five studies were not of interest to this report due to the lack of a comparison between VPT and RC.[6]

Primary Studies

Four primary studies were identified as relevant to this report.[7-10] Three of the studies were RCTs (two single blinded,[7,8] and one multi-centre non-inferiority trial[9]) and one study was a open-label observational cohort study.[10] One study was published in 2018,[7] one in 2017,[8] one in 2015,[9] and one in 2014.[10]

Economic Evaluation

One relevant economic evaluation was identified in the literature search, comparing direct pulp capping (DPC) and RC.[11] The economic analysis was a cost-effectiveness analysis, with a lifetime time horizon and a public-private perspective. A Markov Model was constructed based on a 20-year old male over a lifetime (i.e., model based on these patient characteristics), consisting of initial and follow-up health states. Clinical and costs inputs were found from relevant literature sources.[11]

The following assumptions were identified:

- Direct pulp capping would either be performed successfully, lead to pain, or lead to loss of pulpal vitality.
- RC therapy would be initiated if pain occurred from direct pulp capping, while assuming only a proportion of necrotic pulps would be detected per model cycle. Sensitivity analysis simulated the possibility that some teeth with pain might be extracted rather than restored.
- Pre-existing conditions would lead to four types of therapy: (1) a vital, painless pulp; (2) a vital, painful pulp; (3) a nonvital pulp in a tooth without a radiographically detectable periapical lesion; or (4) a nonvital pulp in a tooth with a periapical lesion. The first would be if RC therapy was initiated directly after pulpal exposure, whereas the other treatments were performed if follow-up treatments were required after DPC.

Country of Origin

The first author of the included SR[6] was from Senegal. The primary studies were based in Turkey,[7] India,[8] Iran,[9] and France.[10] The multicentre-study[9] did not have locations outside of Iran. No Canadian-specific studies were identified.

The country of origin for the economic evaluation was Germany, and the currency was euros.[11]

Patient Population

Systematic Review

The studies eligible for inclusion in the SR were studies that included patients with mature teeth (molars) with irreversible pulpitis.[6] No other specific inclusion or exclusion criteria were provided.

Primary Studies

All included primary studies limited the type of tooth to secondary/permanent dentition.[7-10] The three RCTs[7-9] included patients receiving treatment on molar teeth (maxillary and mandibular). The cohort study included patients receiving treatment on any permanent dentition, including non-molar teeth.[10] All studies were set in a medical university setting.[7-10]

One study limited the population to adults over 18 years of age, and one study limited the population to patients over age nine.[7,9] The remaining studies[8,10] did not limit participants by age.

The eligibility for inclusion or treatment varied. Two studies[7,9] included patients with severe dental pain diagnosed with irreversible pulpitis, one study[8] included periodontically healthy mandibular molars with carious exposure, and one study[10] included patients who had dental care performed under general anesthetic.

One included primary study[9] was a five-year follow-up of two primary studies included in the SR.[6,13,14]

Economic Evaluation

The base case for the economic evaluation was based upon a 20-year male patient with 58.28 years to live with 80% of removed teeth assumed (with 3% discount rate). Subgroups included in the study for the comparison of RC and DPC were older patients (over 40 years of age), patients who had a proximal exposure site instead of an occlusal site, patients with only anterior teeth requiring treatment (excluding posterior teeth), and those patients who were treated with MTA instead of calcium hydroxide mineral trioxide aggregate for DPC.

Interventions and Comparators

All studies included some form of VPT compared with RC.[6-10]

Systematic Review

The SR[6] included studies comparing pulpotomies with different materials (i.e., calcium enriched mixture (CEM), MTA, platelet rich fibrin (PRF), CaOH, or biodentine), and studies comparing pulpotomies with RC. The four studies relevant to this report compared CEM or MTA pulpotomies with RC (the methodology of RC was not reported).[6]

Primary Studies

The interventions in the primary studies were pulpotomy performed with zinc oxide eugenol (ZOE) cement,[7] MTA,[8] or CaOH covered with ZOE,[10] and VPT performed with CEM.[9] Pulpotomy with ZOE was compared to both total and partial pulpectomy.[7] The remaining studies used RC as a comparator.[8-10]

Economic Evaluation

The economic evaluation compared the use of DPC using CaOH to direct restoration with RC therapy followed by a cast coronal restoration.[11]

Outcomes

Pain and clinical success were the most common outcomes included in the studies.

Systematic Review

The outcomes included in the SR[6] were clinical success rate, treatment time span, and adverse events such as inflammation, tenderness to percussion, swelling, and presence of sinus tract. Clinical success rate was defined for one of the included studies in the SR (as absence of symptoms of inflammation, infection, and tenderness to percussion) but was not described for all studies.

Primary Studies

The primary studies included outcomes such as postoperative pain intensity (recorded using a 10 cm visual analogue scale [VAS])[7,8] or dental pain at follow-up (as declared by the patient or patients' carer),[10] thermal pain (absent or present),[7] pain during chewing (absent or present),[7] and analgesic use.[7,8] One primary study focused solely on postoperative pain outcomes in the week following the treatment.[7] One study included postoperative pain in an earlier publication (one year outcomes),[15] but did not include these outcomes in the present report. This was a follow-up report containing data for the five year outcomes.[9] Clinical success rates were recorded in three studies.[8-10] Clinical success was defined in one study as periapical indices (PAIs) of a certain level at varying time periods (e.g., PAI of 1 at time 0 and a PAI of 1 at time 1 – Table 4b includes a full list of definitions of success).[10] Clinical success in another study was defined as a lack of pain, swelling and sinus tract, an intact restoration, and a PAI of 1.[8] The last study provided the conditions that are required to achieve clinical success as remaining pulp being non-inflamed or healing, controlled hemorrhage, the use of a biocompatible capping material, and a bacterial tight seal.[9] However, it was not clear if this specific definition of clinical success was used for the outcome of clinical success in the study, so the definition of clinical success was determined to be not reported.[9]

Economic Evaluation

The outcomes of interest for the evaluation were, cost per retention time of a treated tooth, and time until another endodontic treatment.[11]

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Systematic Review

Overall, the quality of the included SR was very low.[6] The SR was poorly written, with many grammar, spelling, and syntax mistakes, and many mistakes in the reporting of the results (e.g., typos and incorrect values). These mistakes made interpretation extremely difficult and conclusions unclear, and in some cases changed the significance of the results entirely. In some cases, incorrect *P* values and incorrect sample sizes were extracted (as determined by cross-referencing with publications for some of the included primary studies).[6] Conclusions drawn from the stated results did not follow the quantitative numbers

reported, and comparators and outcomes were not clear (e.g., definitions of clinical success were not reported, and what procedures were used for RC were unclear). No information was provided on what the inclusion criteria entailed, aside from “mature teeth with irreversible pulpitis” and which study designs were eligible. Some studies were excluded due to their “full content” not being available, but this was not justified, nor explained why the full texts were not available to the authors.[6]

The authors claimed the evidence in the included RCTs was high quality, despite no critical appraisal for any included study being performed.[6] Additionally, the authors included two studies using the same patient sample (i.e., one is a follow-up study of the other), with no acknowledgement of this, or discussion of the studies as duplicate patients.[6] With no critical appraisal, the authors also did not discuss any bias or heterogeneity in the included studies, and the authors made overall conclusions about pulpotomies using multiple studies, despite each study having a different material used and a different comparator.[6] Overall, results and conclusions from this SR were unclear and should be interpreted with caution.

Primary Studies

Overall, the quality of the included primary studies varied from low to moderate.[7-10]

All included primary studies had well-described aims or objectives and eligibility criteria for patients. In the RCTs, statistical tests were also appropriate for the type of data and outcomes. One study[7] appropriately used medians for non-parametric data and another specifically tested the distributions for normality.[8]

Two studies provided sample size calculations.[7,8] Although the number of teeth included in each study matched the minimum sample sizes required to detect a statistical difference with 80% power and an alpha of 0.05, one study[7] appeared to use 0.001 as the cut off for the alpha (only marking statistical significance on *P* values less than 0.001). Despite this change, this was unlikely to meaningfully change the results of the study, or the interpretation of the *P* values, as the authors provided exact *P* values in the results.[7]

Randomization was done in three of the four studies,[7-9] but the process of randomization was not described in two of these three studies.[8,9] Therefore, the appropriateness of the randomization procedure was unclear. Additionally, one study blinded patients to treatment[7] and two studies concealed allocation (one through sequential envelopes,[7] the other procedure not reported[9]). It was unclear if patients were blinded in one[8] of the included RCTs, and one was an open label design.[9] Blinding of the dentists performing the procedure or clinical assessments was not possible due to the nature of the procedure, but in one RCT[8] assessors were blinded to radiographic treatment results through obscuring of the tooth using Photoshop.

The included cohort study[10] had several limitations in addition to the lack of randomization. The design of the study inherently may have introduced bias as the treatment groups were decided based on clinical signs, so teeth with varying levels of infection may have been more likely to receive one treatment over another.[10] This study also included all locations of teeth, with the proportion of incisors being higher in the RC group when compared with pulpotomy. In the two groups, the loss-to-follow-up was also extremely high. Of all patients that returned for a follow-up at any time (between one month and greater than two years), 64% of patients were lost in the pulpotomy group and 64% in the RC group. No patients in the pulpotomy group returned for follow-up at 24 months or later, so no meaningful comparisons between the groups could be made for long term outcomes for greater than two years. This discrepancy was not justified in the study, so it is unknown if groups

differentially dropped out of later follow-up times due to the treatment or due to other factors. Additionally, no statistical tests were performed on outcomes or on comparative data.[10]

Economic Evaluation

Overall the economic evaluation[11] had a variety of strengths and was well-conducted. The type of economic evaluation, the intervention/comparator and the assumptions made were all clearly specified in the study. Additionally, the sources of the clinical inputs and costs were stated while time horizon and perspective of the analysis were clearly defined. Subgroup and sensitivity analysis were conducted to determine any uncertainty regarding the cost-effectiveness of DPC and RC therapy. However, a few limitations were identified including uncertain generalizability of the study to the Canadian context as the study was based upon a German public-private payer perspective. Additionally, the authors of the economic evaluation constructed a Markov Model based upon a single patient over a life time horizon, which may not be suitable (or representative) of costs or pathways associated with all patients undergoing DPC or RC therapy.[11]

Summary of Findings

Appendix 4 presents a table of the main study findings and authors' conclusions.

Clinical Effectiveness of Vital Pulp Therapy for Mature Teeth

Systematic Review

The SR had four relevant studies with appropriate comparators and outcomes for this report.[6] The sample sizes in each study ranged from 11 teeth to 407 patients, however sample sizes were reported incorrectly for some studies (as confirmed through cross-referencing of included primary studies).

In VPT with CEM compared with RC treatment, there were no significant differences in clinical success at 6 months, 1 year, or 2 years (*P* = NR). In another included study, clinical success (not defined by the authors) after 2 years was 98.18% in both VPT and RC groups.[6] In cases with periapical involvement, "outcomes" were similar between VPT and RC (*P* = 0.117). The results for the outcome of post-operative pain were unclear – the text stated significantly fewer analgesics were taken by patients in the RC group compared with VPT, but the corresponding *P* value does not reflect this (*P* > 0.001). Radiographic results showed significantly different success rates in favour of VPT (*P* = 0.001) at 6 months and 1 year but no significant differences at 2 years.[6]

In VPT with MTA compared with RC treatment, all patients were asymptomatic at follow-up and free of clinical symptoms. There were no changes in the periapical status of the treated teeth, but the sample size was small (11 teeth).

Primary Studies

The primary studies reported on pulpotomies using ZOE,[7] MTA,[8] and CaOH covered with ZOE[10] compared with RC treatments, or VPT performed using CEM[9] compared with RC treatments.

Pulpotomies – ZOE

One study examined pulpotomies using ZOE.[7] There were no significant differences in age, sex or tooth location between groups in the RCT comparing pulpotomies with total or partial pulpectomies ($P = 0.532$, $P = 0.780$, $P = 0.152$ respectively).[7]

For pain relief (difference in VAS), pain levels decreased over time from day 0 to day 7 post-operation in both groups.[7] When comparing total pulpectomy, partial pulpectomy, and pulpotomy, the total pulpectomy group had larger reductions in pain intensity than pulpotomy between day 0 and day 3 and between day 0 and day 7 (both $P < 0.001$).[7]

Chewing sensitivity, thermal sensitivity, and number of analgesics required, were not significantly different between the three groups.[7]

Pulpotomies – CaOH with ZOE

In the one study using CaOH with ZOE, overall (pulpotomy and RC combined), the proportion of successes was 87%, the proportion of uncertain success was 9%, and the proportion of failures was 4%.[10] Patients who were followed up between 1 and 6 months had 95% or 75% proportions of success in the pulpotomy and RC groups respectively. Patients in the 6- to 12-month follow-up groups had successes of 100% and 88% respectively, and patients in the >24-month group has successes of 0% and 90% respectively. The 0% occurred because no patients in the pulpotomy group were followed up with at 2 years (they were all lost to follow-up).[10] This study included 147 adults with cognitive difficulties, 82 patients with dental fear or phobia, and 3 elderly patients with dementia.[10]

Pulpotomies – MTA

One study examined pulpotomies using MTA compared to RC.[8] The median age was significantly different between groups ($P < 0.05$, the pulpotomy group had a younger median age), but there was no significant differences the two groups in the proportions of each sex.

Pain reduction was significant between day 1 to day 4 in the pulpotomy group ($P < 0.05$), but not between day 4 to day 7 ($P > 0.05$). In the RC group, pain reduction was significant between day 2 to day 7 ($P < 0.05$), but not from day 1 to day 2 ($P > 0.05$).[8]

Overall clinical success was not significantly different between RC treatment and pulpotomy (87.5% versus 84.6%, $P = 0.951$). Two patients in the pulpotomy group required follow-up RC therapy at 6 months, and one required RC therapy at 9 months. Two patients in the RC group had treatment labeled as a failure.[8]

Vital pulp therapy – CEM

One study examined VPT with CEM compared to RC. This study was a five-year follow-up of an RCT, with one-year and two-year results published elsewhere.[13,14] The authors of the study did not reported statistical analysis of baseline demographics and did not report the mean or median age of patients in the study, despite doing subgroup analyses using age.[9] These may have been published in the previous reports. Patient age and gender were found to be not significantly related to treatment outcome in either VPT or RC groups ($P = 0.72$ and 0.61 for age respectively, $P = 0.244$ and 0.731 for gender, respectively).

Overall success of VPT and RC over 5 years was 78.1% and 75.3% respectively (not significantly different between groups; $P = 0.61$), with an overall loss to follow-up of 136 patients (33.4%).[9]

Cost-Effectiveness of Vital Pulp Therapy for Mature Teeth

In the included economic evaluation, DPC was significantly higher in cost-effectiveness than RC treatment in the base case (ICER = €–516.11/retention years).[11] DPC was never costlier than RC and remained more cost-effective, even with differing willingness to pay thresholds (ceiling values from 0 to 250 euro) and despite DPC having an overall shorter mean time before follow-up treatment was required.. However, this analysis was based on one patient, and not on an RCT or larger study, so results should be interpreted with caution.[11]

In sensitivity analyses, DPC was more expensive and less effective in teeth that had a proximal exposure site instead of an occlusal exposure site, and in patients over 40 years of age. Neither treatment dominated (i.e., was both less costly and more effective) in a subgroup analyses of anterior-only teeth.[11]

Guidelines

No relevant guidelines regarding VPT for mature teeth were identified; therefore, no summary can be provided.

Limitations

One limitation of the included evidence in this report is the limited generalizability to the Canadian context. None of the included studies were conducted in Canada or in the Canadian population, and none of the studies were based in North America. The included economic evaluation[11] was based on a German system and costing data and may not reflect current Canadian pricing.

The only materials included in this report with comparative data to RC were CEM, ZOE, CaOH with ZOE, and MTA. Despite having four materials, there was only one primary study per material, and studies using other materials such as biodentine, adhesive resins, and resin modified glass ionomers were not identified in the literature. Therefore, conclusions regarding VPT performed with these alternative materials cannot be made.

Outcomes in the included studies were most commonly clinical successes and pain, but pain outcomes were generally short-term (1 week) and “clinical success” was not defined or inconsistently defined across studies. Therefore, with the different interventions present in this report and the differing outcomes, comparing the interventions across studies is not possible. Additionally, the quality of the included studies was variable, ranging from very low to moderate, which may limit the certainty in the results and conclusions.

Finally, a limitation of the present study was the lack of “real-world” settings included in the studies. All of the primary studies[7-10] were set in medical university settings, which may not reflect the settings in which majority of care is received by Canadians and specific Canadian subgroups (such as the military).

Conclusions and Implications for Decision or Policy Making

Six studies (one SR,[6] four primary studies,[8-10,16] and one economic evaluation) were identified regarding vital pulp therapies for mature teeth.

Overall, when comparing VPT and RC, short-term pain reduction was more pronounced in teeth receiving total pulpectomy compared with partial pulpectomy or pulpotomies using

ZOE, but pain significantly subsided over time in all groups.[7] In pulpotomies with MTA, pain significantly subsided earlier than in the RC group.[8]

In comparisons of clinical success between MTA pulpotomies and RC, the proportion of success did not significantly differ between groups.[8] Clinical success was also not significantly different between VPT with CEM and RC.[9] The highest proportions of failure in the included studies were 21.9% and 24.7% for VPT and RC respectively over five years.[9]

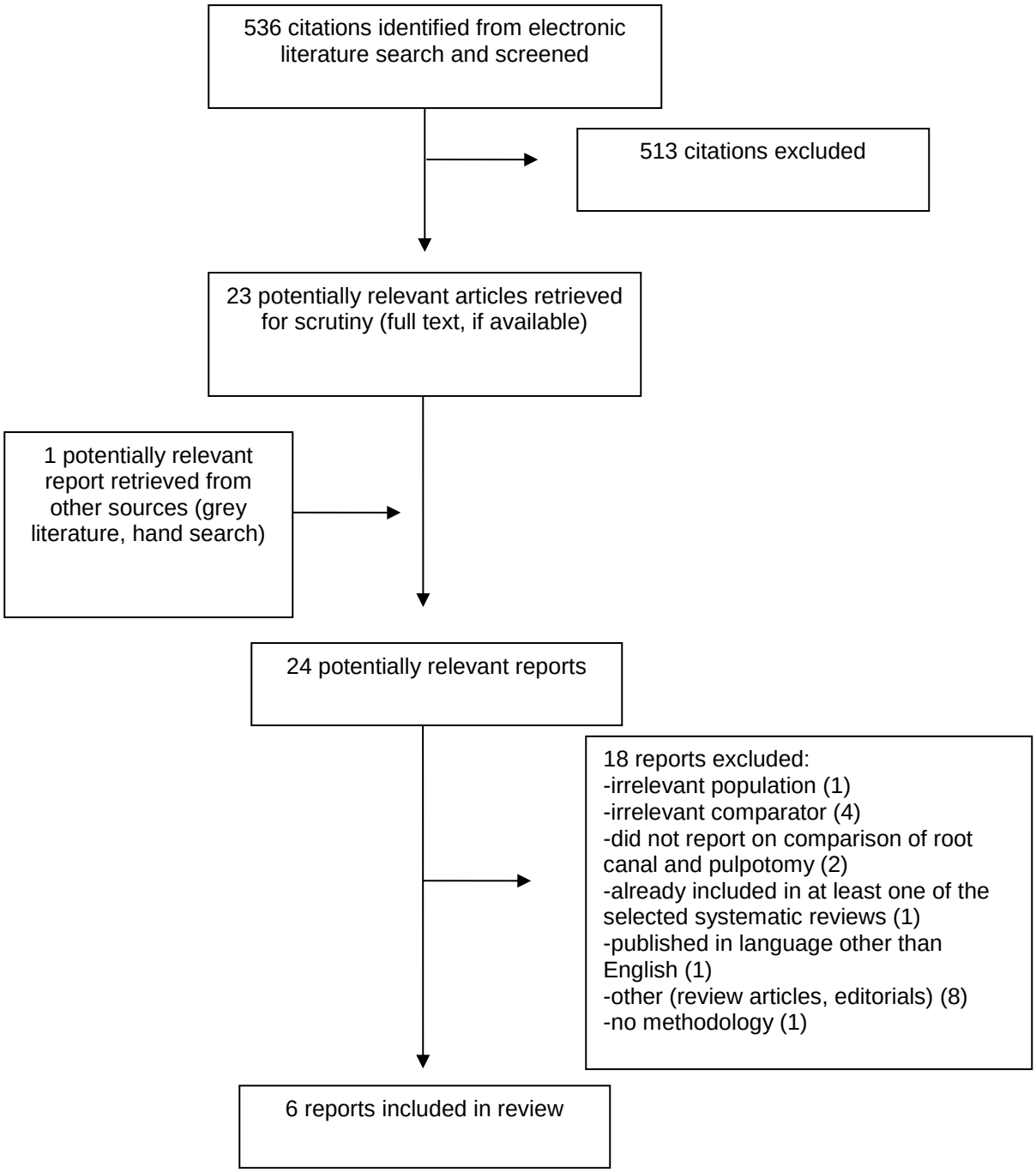
In a German context, DPC appeared to be cost-effective when compared to RC over a lifetime time horizon, and this result was maintained with variable willingness-to-pay thresholds (ceiling values between 0 and 250 euros).[11] In sensitivity analyses, DPC was found to not be cost-effective in patients over 40 years of age and in teeth with a proximal pulp exposure site.[11]

These results have many limitations, including uncertainty due to low quality of evidence, low generalizability to the Canadian context, lack of evidence for some types of VPT (e.g., no studies using biodentine), and a high variety of techniques used (e.g., different dentists using different preparations or anesthetics, different techniques required for different materials used). Further research addressing these limitations, including larger scale RCTs or research conducted in a Canadian context may help reduce uncertainty in the findings.

References

1. Morotomi T, Washio A, Kitamura C. Current and future options for dental pulp therapy. *Jpn Dent Sci Rev.* 2019;55(1):5-11.
2. Ghoddusi J, Forghani M, Parisay I. New approaches in vital pulp therapy in permanent teeth. *Iran Endod J.* 2014;9(1):15-22.
3. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358:j4008. http://www.bmj.com/content/bmj/358/bmj.j4008.full.pdf. Accessed 2019 Jul 10.
4. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52(6):377-384. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf. Accessed 2019 Jul 10.
5. Higgins JPT, Green S, editors. Figure 15.5.a: Drummond checklist (Drummond 1996). In: *Cochrane handbook for systematic reviews of interventions.* London (GB): The Cochrane Collaboration; 2011: http://handbook-5-1.cochrane.org/chapter_15/figure_15_5_a_drummond_checklist_drummond_1996.htm. Accessed 2019 Jul 10.
6. Seck A, Kaboré WAD, Ndiaye D, Ndiaye I, Benoist FL. Radiological and clinical assessment of pulpotomy on mature permanent molars with irreversible pulpitis: literature review *IP Indian J Conserv Endod.* 2018;3(4):104-115.
7. Eren B, Onay EO, Ungor M. Assessment of alternative emergency treatments for symptomatic irreversible pulpitis: a randomized clinical trial. *Int Endod J.* 2018;51 Suppl 3:e227-e237.
8. Galani M, Tewari S, Sangwan P, Mittal S, Kumar V, Duhan J. Comparative evaluation of postoperative pain and success rate after pulpotomy and root canal treatment in cariously exposed mature permanent molars: a randomized controlled trial. *J Endod.* 2017;43(12):1953-1962.
9. Asgary S, Eghbal MJ, Fazlyab M, Baghban AA, Ghoddusi J. Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial. *Clin Oral Investig.* 2015;19(2):335-341.
10. Cousson PY, Nicolas E, Hennequin M. A follow-up study of pulpotomies and root canal treatments performed under general anaesthesia. *Clin Oral Investig.* 2014;18(4):1155-1163.
11. Schwendicke F, Stolpe M. Direct pulp capping after a carious exposure versus root canal treatment: a cost-effectiveness analysis. *J Endod.* 2014;40(11):1764-1770.
12. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.
13. Asgary SE, M.J. Treatment outcomes of pulpotomy in permanent molars with irreversible pulpitis using biomaterials: a multi-center randomized controlled trial. *Acta Odontol Scand.* 2013(71):130–136.
14. Asgary S, Eghbal MJ, Ghoddusi J. Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial. *Clin Oral Investig.* 2014;18(2):635-641.
15. Asgary S, Eghbal MJ, Ghoddusi J, Yazdani S. One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial. *Clin Oral Investig.* 2013;17(2):431-439.
16. Bahrololoomi Z, Fekrazad R, Zamaninejad S. Antibacterial effect of diode laser in pulpectomy of primary teeth. *J Lasers Med Sci.* 2017;8(4):197-200.

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2a: Characteristics of Included Systematic Review

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Seck, 2018[6] **Senegal**	9 included studies; 4 studies with comparisons relevant to the present report RCTs, non-randomized studies, clinical trials, case reports, longitudinal studies	Mature permanent molars with irreversible pulpitis	Intervention: Pulpotomy (CEM, MTA, PRF, CaOH, Biodentine) Comparator: Root canal	Clinical success rate, treatment time span, tenderness, inflammation, post-operative pain, clinical signs/symptoms (pain, swelling, presence of sinus tract, tenderness to percussion) One week to 42 months

CaOH = calcium hydroxide; CEM = calcium enriched mixture; MTA = mineral trioxide aggregate; PRF = platelet rich fibrin; RCT = randomized controlled trial.

Table 2b: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Eren 2018[7] **Turkey**	Single-blinded, single-centre RCT	Patients 18 to 60 years of age with severe dental pain in the posterior maxillary or mandibular molar teeth, diagnosed with symptomatic irreversible pulpitis with or without symptomatic apical periodontitis N = 66 No patients LTF	Pulpotomy (ZOE cement) (n=22) Total pulpectomy (n=22) Partial pulpectomy (n=22)	Preoperative pain intensity, postoperative pain intensity (VAS score), pain upon chewing, pain upon thermal stimulus, analgesic use 7 days of follow-up (Day 0, 1, 3 and 7)
Galani 2017[8] **India**	Single blinded RCT	Patients with periodontally healthy first and second permanent mandibular molars with carious exposure of pulp. N = 54 LTF = 4	Pulpotomy (MTA) (n= 26) RC therapy (n = 24)	Post-operative pain, success rate, analgesic use 7 days *Treatment success was defined as lack of pain, swelling and sinus tract, intact restoration, radiographs with PAI of 1*

Table 2b: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Asgary 2015[9] **Iran**	Non-inferiority multicenter RCT	Patients who had a vital molar tooth with a history of pain indicative of irreversible pulpitis and those who had opted for extraction for pain relief and announced to be prepared for future recalls. N = 407 LTF = 136	VPT (CEM) (n = 137) RC therapy (n = 134)	Clinical success rate, radiographic success rate, treatment failure 60 months
Cousson 2014[10] **France**	Open, observational cohort study	Any patient with one endodontic treatment on a permanent tooth during a previous dental care session under GA N = 646 endodontic treatments N = 250 patients 32 treatments excluded LTF (1 to 6 months)[a] = 540 LTF (>6 to 24 months) [a] = 537 LTF (> 24 months) [a] = 537	Pulpotomy (calcium hydroxide covered with ZOE) (n = 87) Root canal treatment (n = 527)	Tooth present in arch, dental pain, pain related behaviours, clinical symptoms of infection (edema, fistula, tooth motility) *Success defined as a periapical index (PAI) of:* • *1 at Time 0 and 1 at Time 1* • *2 at Time 0 and ≤ 2 at Time 1* • *3 at Time 0 and ≤ 2 at Time 1* • *4 at Time 0 and ≤ 3 at Time 1* • *5 at Time 0 ≤ 4 at Time 1* *Time 0 was the time of the postoperative radiographic control at the end of the endodontic treatment* *Time 1 was the time of radiographic control after the longest follow-up examination period*

CEM= calcium-enriched mixture; GA = general anesthetic; LTF = lost to follow-up; MTA = mineral trioxide aggregate; PAI = periapical index; PG = pulpotomy group; PP = partial pulpotomy; RC = root canal; RCT= randomized controlled trial; TP = total pulpotomy; VAS = visual analogue scale; VPT= vital pulp therapy; ZOE = zinc oxide and eugenol.

[a] Loss to follow-up from cohort of 614 endodontic treatments.

Table 2c: Characteristics of Included Economic Evaluations

First Author, Publication Year, Country	Type of Analysis, Time Horizon, Perspective	Decision Problem	Intervention and Comparator(s)	Clinical and Cost Data Used in Analysis	Main Assumptions
Schwendicke 2014[11] **Germany**	CEA Life time horizon German public-private-payer perspective	"Aimed to assess the cost-effectiveness of both direct capping and RC… for pulps being exposed during caries removal. Cost-effectiveness was evaluated for different subgroups and clinical situations, and the robustness of our findings was determined." (Page 1)	DPC RC	- Costs were based on German health care costs - Model parameters were based on literature sources	- DPC could be performed successfully or lead to pain or loss of pulpal vitality (i.e., pulpal necrosis). Assuming the latter to be associated with bacterial infection, it could eventually lead to the development of a radiographically detectable periapical lesion. - In case of pain after DPC, RC treatment was to be initiated. - Only a certain proportion of necrotic pulps would be detected per cycle. - Four types of RC were simulated based on pre-existing conditions

CEA = cost-effectiveness analysis; DPC = direct pulp capping trial; RC = root canal.

Appendix 3: Critical Appraisal of Included Publications

Table 3a: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2[3]

Strengths	Limitations
Seck, 2018[6]	
- More than two databases used for systematic search, with manual searching performed - Language restrictions outlined - Eligibility of study designs clearly outlined	- Many spelling errors and grammatical errors, making understanding difficult (e.g., P000.1 written instead of P = 0.001) - Writing was very poor, making the conclusions difficult to interpret or understand. There were links to tables and figures that are not available in the report. - Incorrect conclusions drawn for some statistics, either due to spelling errors or incorrect extraction - No justification for language restriction, limited keywords used for search (unclear if MeSH terms used) - Seven articles out of possible sixteen were excluded due to "full content not available" – unclear whether this was because articles were not freely available, too expensive, or another reason - Unclear inclusion criteria components for study eligibility - No information on duplicate data extraction or abstract screening - No information on critical appraisal of included studies (unlikely to have been done) - Populations of included studies unclear (age, demographics, more information on procedure used for pulpotomy, location of teeth) - No information on procedure used for comparator of root canal - Limited information on definition of "clinical success" for included studies - Incorrect sample sizes reported in results table (e.g., 75 patients reported for Asgary 2014,[14] when 332 patients were included in this study) - No information regarding conflicts of interest reported - No discussion of heterogeneity or bias in conclusions - No acknowledgement that two of the included studies were the same patient sample (one was a 2-year update of the previous study)

Table 3b: Strengths and Limitations of Clinical Studies using Down's and Black Checklist[4]

Strengths	Limitations
Eren 2018[7]	
- Aim/objective of the study clearly described - Sample size calculated for main outcome, with appropriate sample size recruited	- Cut-off of $P < 0.05$ determined as significant in methods, but $P < 0.001$ used in results.

Table 3b: Strengths and Limitations of Clinical Studies using Down's and Black Checklist[4]

Strengths	Limitations
- Randomization sequence outlined, using a random number generator at a 1:1:1 allocation ratio - Allocation concealed using sequentially numbered envelopes - Actual probability values recorded - Main outcomes with scales outlined - Inclusion and exclusion criteria clearly outlined - No loss to follow-up (likely because of the short follow-up time) - All procedures performed by the same operator, which may help eliminate operator-related confounding - No issues of compliance with procedure, as the patient cannot remove or modify the tooth themselves - Patients blinded to treatment received (unable to blind operator due to nature of the procedure) - Procedures performed clearly stated - Validated VAS 10 cm scale used to assess pain - Assuming non-parametric data (group results seem to indicate this is likely), appropriate non-parametric (Kruskal Wallis, Conover's) test used with medians - Conflicts of interest (none) clearly stated - Some demographic information included	- Medians used for statistical testing, but this was not justified, nor was the distribution of data discussed (parametric or non-parametric) - Very short follow-up (one week) with no outcomes regarding tooth integrity or procedure success, so limited conclusions to be made for long term follow-up - Not all relevant demographic information presented
Galani 2017[8]	
- Aim/objective of the study clearly described - Clear inclusion and exclusion criteria - Concealed allocation using envelopes - Sample size calculated for main outcome, with appropriate sample size recruited - Clinical procedure described in detail - Validated VAS 10 cm scale used to assess pain, with detailed definitions of mild, moderate, and severe pain - Assessors of radiographic evaluations blinded to treatments, two independent endodontic assessors assessed radiographs - Small loss to follow-up over long term - Distribution of data tested for normality, found to be non-parametric. Appropriate non-parametric tests (Mann Whitney U for intergroup comparisons, Wilcoxon signed rank test for intra-group comparisons) were then used to analyse the data - All procedures performed by the same operator, which may help eliminate operator-related confounding - No issues of compliance with procedure, as the patient cannot remove or modify the tooth themselves - Kappa values for interrater agreement were calculated and were good	- Randomization done, but methodology not described - Significant difference in age between two comparator groups ($P < 0.05$) - Pain intensity displayed in a graphical form, without accompanying numbers or *P* values. - Inconsistent reporting. Abstract stated significant difference in pain incidence between groups, but within text, only 24-hour pain incidence reported (which was non-significant). 1st day intergroup comparison in table was significant. - Some results/outcomes not reported (e.g., number of patients using analgesics) - Severity of carious exposure not described or statistically tested between groups - Not stated whether patients were blinded to treatment - Patients recruited from one university post-graduate department referrals, so may not be representative of common practice
Asgary 2015[9]	
- Aim/objective of the study clearly described - Clear inclusion and exclusion criteria	- Open labelled design - Process of randomization not described - Not all relevant demographic information presented

Table 3b: Strengths and Limitations of Clinical Studies using Down's and Black Checklist[4]

Strengths	Limitations
- No significant difference in follow-up times found between groups - Patients recruited from a variety of centres, which may make them more representative of general population - COI reported (none) - Loss to follow-up addressed, bias unlikely to have affected results - Treatment performed by general dentists, which may reflect regular treatment and be more representative of the general population - Specific *P* values reported	- Statistical analysis conducted unknown (referred to as "the statistical analysis") - Many study details referred to initial 2013 study, but not presented here - Despite acknowledging socioeconomic status as a potential confounding factor in dental study, did not report on the socioeconomic status of participants - Treatment performed by general dentists, who may not be as experienced with the procedures
Cousson 2014[10]	
- Aim of study clearly described - To prevent confounding and ensure similar procedures for patients, patients who had received endodontic treatment under general anaesthesia in another dental service were not included. - Criteria for success, failure, and uncertainty clear - Validated/prepared forms used for endodontic case difficulty, periapical status etc. - Internal reliability for radiograph evaluation tested with Cohen's Kappa	- Received non-identical treatments/follow-up. Some patients returned regularly, and some based on whether patient had problems or infection. Some patients examined under analgesia, some examined awake - Patients were not randomized to treatment groups – treatment likely was decided on based on clinical signs (a more infected tooth was more likely to be given a root canal treatment) - No demographic information described or statistically tested, unsure if groups receiving either treatment were comparable (especially with no randomization of treatment groups) - Patients were not blinded to receipt of treatment, so may have reported different pain symptoms - Sample sizes not calculated for outcomes relevant to this report - Very large loss to follow-up (224 treatments not examined again [no specified reason], some patients [65 treatments] could not cope with radiographic evaluation), and reasons for loss to follow up were not reported. Loss to follow-up may have been due to successful treatments, or non-cooperation with check-ups (these patients may have had problems with the procedure) - Pulpotomy therapy groups had significantly (*P* < 0.001) higher "case difficulty" and RC groups had worse "pulpal status", which may have contributed to the lower success rate - Inconsistency in reporting; some numbers do not match – i.e., the endodontic case difficulty intergroup comparison was significant in text, but not significant in the table - Large loss to follow-up in both groups (64%). No pulpotomies were followed up in > 2-year time frame (all 87 lost to follow-up) - No statistical analysis on results for comparative data, or on intra-group comparisons, therefore conclusions were uncertain

Table 3b: Strengths and Limitations of Clinical Studies using Down's and Black Checklist[4]

Strengths	Limitations
	- Larger proportion of incisors/canines included for RC group (53% of cohort), when compared to pulpotomy (2%). Larger numbers of molar included for pulpotomy (96% of cohort) when compared to RC therapy (24%) - Specific *P* values not reported

Table 3c: Strengths and Limitations of Economic Study using the Drummond Checklist[5]

Strengths	Limitations
Schwendicke, 2014[6]	
- Economic evaluation type specified - Assumptions were clearly stated - Comparator and intervention clearly stated in the analysis - Model based analysis - Time horizon and perspective of analysis defined - Discount rates and currency identifiable - Data and costs outcomes were stated - Sensitivity analysis conducted to determine uncertainty regarding the effectiveness of DRC and RC - ICER clearly reported as well as the interpretation of the ICER results	- Study may not be generalizable to the Canadian context as the analysis was based on German private public payer perspective - Markov model was constructed based on single male patient over a lifetime

DPC= direct pulp capping trial; ICER: = incremental cost effectiveness ratio; RC = root canal.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 4a: Summary of Findings of Included Systematic Review

Main Study Findings	Authors' Conclusion
Seck, 2018[6]	
4 studies out of the included 9 studies were relevant to the comparison of pulpotomy compared to root canals - 2 of these 4 studies were the same patient base (one is one-year follow-up, the other is two-year follow-up) Sample size in each study ranged from 11 teeth to 407 patients Follow-up periods ranged from one week to 42 months **<u>VPT with CEM vs. RC therapy, permanent molars, irreversible pulpitis</u>** **Clinical controls** *Clinical success (absence of symptoms of inflammation, infection, tenderness to percussion):* - No significant differences at 6 months, 1 year, and 2 years (P = NR, n = 385) *Clinical success (not defined), VPT vs. RC therapy* - At 2 years, 98.19% in both groups - "Outcomes in cases with preoperative periapical involvement were similar", *P* = 0.117 - 6 months, 98.3% vs. 94.4% (*P* > 0.05) - 1 year, 97.6% vs. 91.3% (*P* > 0.05) *Post-operative pain, number of painkillers taken* - Significantly fewer in RC therapy group than VPT, but *P*-value reported as *P* > 0.001[a] **X-ray (radiographic) controls** *Success rates, VPT vs. RC therapy* - 6 months (four examiners), significant difference *P* = 0.001[c] (in favour of VPT) - 1 year (four examiners), significant difference *P* = 0.001[c] (in favour of VPT) - 1 year, 92.2% vs. 70.3% (*P* = 0.001) - 2 years, 86.7% vs. 79.5% (*P* = 0.053) - Presence of radiographic periapical lesions did not significantly affect success rate in VPT but did in RC therapy group – at 6 and 12 months, *P* = 0.001[c] *Quality of treatment, Strindberg Criteria, VPT vs. RC therapy* - 92.8% vs. 66.3% with good quality treatment, *P* < 0.001 - *"significant relationship between the quality of treatment and one-year post-operative radiographic success rates" Page 109* *Radiographic evaluation, four examiners* - "Overall consensus" was no statistically significant difference at 2 years, *P* = NR[b]	*"There was high-quality and long-term evidence from multicenter randomized clinical trials to support the use of VPT/CEM new biotechnology instead of RC… for patients suffering from irreversible pulpitis. Data relating to pain relief effect, radiographic outcomes, safety, costs, availability, accessibility and impact of VPT/CEM biotechnology, demonstrated superiority of VPT/CEM over RC... We can conclude that VPT with a bio-regenerative material can be recommended for general clinical practice worldwide" Page 108-109* *"Two-year treatment outcomes of VPT/CEM are statistically non-inferior to one-visit RC… in human mature molar teeth with established irreversible pulpitis." Page 108* *"In conclusion, pulpotomy using MTA could be a good alternative for RC… for managing symptomatic mature permanent teeth with carious exposure." Page 111*

Table 4a: Summary of Findings of Included Systematic Review

Main Study Findings	Authors' Conclusion
Preoperative periapical involvement, baseline, VPT vs. RC therapy - N = 63 vs. n = 65, *P* = NS - 31% overall (128 patients) **<u>VPT with MTA vs. RC therapy, carious exposure, tooth location NR, tooth condition NR (assumed to be irreversible pulpitis as this was research question of SR)</u>** N = 11 teeth **Clinical controls** - All patients asymptomatic at follow-up - All patients free of clinical symptoms (pain, swelling, sinus tract issues, tenderness) at follow-up **X-ray (radiographic) controls** - No changes in periapical status of treated teeth	

CEM = calcium enriched mixture; MTA = mineral trioxide aggregate; NR = not reported; NS = not significant; RC = root canal; SR = systematic review; VPT = vital pulp therapy.

[a] Report states significance, despite a *P* value of greater than 0.001. Specific *P* value not reported.

[b] Unclear if consensus was quantitatively examined or radiographic examiner's consensus

[c] Written in the report as "P000.1". Assumed to be P = 0.001. Report then links to a "table 2" for this statistic that does not exist in the report. In the follow-up study, the same follow-up time was written as P = 0.001.

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Eren 2018[7]	
<u>Demographics</u> *Age (years ± SD), TP vs. PP vs. Pulpotomy* - 35.7 ± 9.3 vs. 34.0 ± 13.6 vs. 37.8 ± 9.9 - *P* = 0.532 *Sex (n), TP vs. PP vs. Pulpotomy* - Male: 10 vs. 10 vs. 8 - Female: 12 vs. 12 vs. 14 - *P* = 0.780 *Tooth type/location (n), TP vs. PP vs. Pulpotomy* - Mandibular molar: 13 vs. 8 vs. 14 - Maxillary molar: 9 vs. 14 vs. 8 - *P* = 0.152 **<u>Pain relief (difference in VAS)</u>**	*"In all three treatment groups, pain intensity decreased consistently over time… When the treatment groups were compared, the total pulpectomy group reported larger reductions in pain intensity than the pulpotomy group between Days 0 and 7, Days 1 and 3, and Days 1 and 7 (P < 0.001 for all; Table 2). No other intergroup differences were noted regarding changes in pain intensity" Page e231* *"As emergency treatments for cases of irreversible pulpitis with or without periapical changes on radiographs, pulpotomy, partial pulpectomy and total pulpectomy were similar with respect to pain relief, reduction in thermal and chewing sensitivity, and postoperative analgesic use. In a busy clinical setting with limited time for emergencies, pulpotomy may be preferred because it requires significantly less time and is a simple technique that relieves symptoms effectively." Page e236*

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Pain relief assessed from pre-operation (baseline) to day 7 post-operation (day 0 = day of operation, post-operation) **Pain (VAS; median), TP group:** - pre-op (8), day 0 (6), day 1 (4.5), day 3 (1), day 7 (0) - *P* < 0.01 for pre-op vs. day 1, day 3, and day 7 - *P* < 0.01 for day 0 vs. day 1, day 3, and day 7 - *P* < 0.01 for day 1 vs. day 3, and day 7 **Pain (VAS; median), PP group:** - **Pre-op (8), day 0 (4), day 1 (2), day 3 (0), day 7 (0)** - *P* < 0.01 for pre-op vs. day 0, day 1, day 3, and day 7 - *P* < 0.01 for day 0 vs. day 3 and day 7 **Pain (VAS; median), pulpotomy group:** - Pre-op (8), day 0 (2), day 1 (1), day 3 (1), day 7 (0.5) - *P* < 0.01 for pre-op vs. day 0, day 1, day 3, and day 7 - *P* < 0.01 for day 0 vs. day 3 and day 7 **Difference in VAS score, inter-group comparisons, TP vs. PP vs. pulpotomy** - Pre-op to day 0: –1.5 vs. –4 vs. –6, *P* = 0.017 - Pre-op to day 7: –8 vs. –7.5 vs. –7, *P* = 0.046 - Day 0 to Day 3: –3.5 vs. –2 vs. –1, *P* = 0.020 - Day 0 to Day 7: –5.5 vs. –3 vs. –1, *P* < 0.001 ○ (significant difference between TP and pulpotomy) - Day 1 to Day 3: –1.5 vs. 0 vs. 0, *P* < 0.001 ○ (significant difference between TP and pulpotomy) - Day 1 to Day 7: –2.5 vs. –1.5 vs. 0, *P* < 0.001 ○ (significant difference between TP and pulpotomy) - Day 3 to Day 7: –1 vs. 0 vs. 0, *P* = 0.010 Difference in VAS score (i.e., pain relief) comparison between TP, PP, and pulpotomy pre-op to day 1 and pre-op to day 5, non-significant (*P* > 0.05) **<u>Other clinical outcomes</u>** **Chewing sensitivity (%)** Pre-op vs. day 7, TP, *P* < 0.001 Day 0 vs. day 7, TP, *P* < 0.001 Pre-op vs. day 7, PP, *P* < 0.001 Pre-op vs. day 1, day 3, day 7, pulpotomy, *P* < 0.001 All other comparisons NS (including inter-group comparisons) **Thermal sensitivity, TP, intra-group scores** - Pre-op vs. day 0, day 1, day 3, day 7, *P* < 0.001 **Thermal sensitivity, PP, intra-group scores** - Pre-op vs. day 1, day 3, day 7, *P* < 0.001	

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Thermal sensitivity, pulpotomy, intra-group scores - Pre-op vs. day 0, day 1, day 3, day 7, *P* < 0.001 Inter-group comparisons NS **Postoperative analgesic use** Intergroup difference, proportion of patients taking at least 1 analgesic, *P* = 0.277 Intergroup difference, tablets required per patient, *P* = 0.365	
Galani, 2017[8]	
<u>Demographics:</u> Total N = 50 Intervention vs. Comparator Pulpotomy (n = 26) vs. RC (n = 24) *Sex:* Female (n = 24/50) vs. Male (n = 26/50) - *P* > 0.05 *Median Age:* Pulpotomy (20 years) vs. RC (23 years) - *P* < 0.05 **<u>Clinical Outcomes</u>** Pain incidence, RC vs. pulpotomy - 24 hours: 100% vs. 70.3%, *P* = 0.05 **Pain Reduction** • Pulpotomy group had significant (*P* < 0.05) pain reduction from day 1 to day 4 • Pulpotomy group had non-significant pain reduction day 4 to day 7 • RC group had non-significant pain reduction day 1 to day 2 • RC group had significant pain reduction (*P* < 0.05) from day 2 to day 7 ○ Note: Both groups were evaluated on the same days; only the above time point comparisons were reported **Interappointment Pain Score (VAS scale ± SD), RC vs. pulpotomy:** Preoperative: 3.32 ± 0.98 vs. 3.81 ± 1.3 - *P* = 0.096 Day 1: 2.84 ±1.97 vs.1.52 ± 1.28	*"…mean pain scores decreased in both groups, with the pulpotomy group experiencing less pain compared with the RC…. group on all days. Most patients had either no pain or mild pain by the second day postoperatively in the pulpotomy group, whereas mild to moderate pain persisted in the RC…group until the fourth day" Page 1957* *"The mean postoperative pain scores were statistically significantly lower for the pulpotomy group, indicating more symptomatic relief in the pulpotomy group. Thus, it can be concluded that pulpotomy can be an alternative treatment for emergency relief of pain." Page 1958* *"Within the limitations of the study, it can be suggested that coronal pulpotomy can serve as a suitable alternative treatment option for cariously exposed permanent teeth with no signs of apical periodontitis" Page 1961*

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
- *P* = 0.011 Day 2: 2.52 ± 2.12 vs. 0.59 ± 0.70 - *P* = 0.000 Day 3: 1.64 ± 2.01 vs. 0.30 ± 0.60 - *P* = 0.008 Day 4: 1.20 ± 1.58 vs. 0.15 ± 0.36 - *P* = 0.007 Day 5: 0.68 ± 1.07 vs. 0.04 ± 0.19 - *P* = 0.001 Day 6: 0.44 ± 0.82 vs. 0.00 - *P* = 0.004 Day 7: 0.12 ± 0.33 vs. 0.00 - *P* = 0.066 Mean VAS score: 3.32 ± 0.98 vs. 3.81 ± 1.3, *P* > 0.05 **Overall Success Rates, pulpotomy vs. RC, number of patients (%)** One patient in each group LTF for success follow-up *Note: treatment success was defined as lack of pain, swelling and sinus tract, intact restoration, radiographs with PAI of 1* - Success: 22 (84.6) vs. 21 (87.5), *P* = 0.951 - Uncertain: 1 vs. 1 - Failure: 3 vs. 2 (two patients in pulpotomy group required RC at 6 months, one at 9 months) **Analgesic Use** - *P* < 0.05 in favour of pulpotomy group (no patients in pulpotomy group took analgesics, some in RC group took analgesics, number NR)	
Asgary, 2015[9]	
Demographics Total N = 271 Intervention vs Comparator VPT/CEM (n = 137) vs. RC (n = 134) *Sex* Female: VPT/CEM (n = 93) vs. RC (n = 86) Male: VPT/CEM (n = 44) vs. (n = 48) *Mean age* Not specified	*"Outcome and patients' age were not significantly related in each of the defined age groups" Page 337* *"The impact of gender on outcomes of treatment in each of the study arms, the statistical analysis did not reveal a significant difference" Page 337* *"For the interaction of treatment type and preoperative periapical involvement of the teeth on treatment success and Failure" Page 337*

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Clinical results **Overall success, VPT vs. RC therapy, %** - 78.1 vs. 75.3, *P* = 0.61 **Subgroup analyses** *Treatment success in different age groups, number (%)* *VPT/CEM group* < 20 years: 24 (75) 21 -29 years: 48 (81.4) ≥30 years: 35 (76.1) - *P* = 0.72 *RC group* < 20 years: 17 (68) 21- 29 years: 53 (77.9) ≥ 30 years: 31 (75.6) - *P* = 0.61 *Treatment success by gender* *VPT/CEM group* Female: 70 (75.3) Male: 37 (84.1) - *P* = 0.244 *RC group* Female: 64 (74.4) Male: 37 (77.1) - *P* = 0.731 *The main effect of PPI on outcomes* *VPT/CEM group* PPI (-): 82.4% successes PPI (+): 65.7% successes - *P* = 0.71 *RC group* PPI (-): 80.4% successes PPI (+): 66.7% successes - *P* = 0.71	*"The 5-year success rate of VPT/CEM was comparable to that of RC; in other words, for the treatment of irreversible pulpitis, VPT/CEM approach is not only non-inferior to RC, but also, it ended up in equivalent results compared to RC" Page 337* *"PPI around the target teeth did not affect the outcomes of VPT, as many of the samples in the VPT/CEM group did show a preoperative periapical involvement, and the presence of these lesions did not influence the positive treatment outcomes." Page 338* *"...treatment outcomes of VPT/CEM in mature permanent molars with established irreversible pulpitis is comparable with RC" Page 339*
Cousson 2014[10]	
Demographics *Mean age ± SD* Female: 29.2 ± 14.5 years Male: 26.8 ± 12.4 years *Sex* Female: 127 Male: 123	*"Among the 32 pulpotomies in the follow-up group, 31 were considered as "success" while one case of immature tooth was still uncertain (Table 3). Considering the rough evaluation of the pulpal status and the procedural conditions based on the use of calcium hydroxide and ZOE, this rate seems rather high. The high success rate for pulpotomy could be related to good aseptic procedures based on the rubber dam isolation and the abundant irrigation with sodium hypochlorite and the good seal offered by pre-formed crowns. This study suggests that*

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
147 adults had mental or cognitive deficiencies, 71 adults and 11 adolescents had dental fear or phobia, six adults were medically indicated for GA and three elderly persons had dementia. Type of tooth, overall (whole cohort), number (%): - Incisor/Canine: 283 (46) - Premolar: 123 (20) - Molar: 83 (34) Type of tooth, overall (follow-up), number (%): - Incisor/Canine: 114 (51) - Premolar: 44 (20) - Molar: 67 (29) Overall cohort (both pulpotomy and RC), *P* = NS **Clinical outcomes** *Success defined as a periapical index (PAI) of:* • *1 at Time 0 and 1 at Time 1* • *2 at Time 0 and ≤ 2 at Time 1* • *3 at Time 0 and ≤ 2 at Time 1* • *4 at Time 0 and ≤ 3 at Time 1* • *5 at Time 0 ≤ 4 At Time 1* *Time 0 is the time of the postoperative radiographic control at the end of the endodontic treatment* *Time 1 is the time of radiographic control after the longest follow-up examination period* **Overall** - 87% success - 9% uncertain - 4% failure *Note: Treatments were distributed into "follow-up" categories based on when patients returned for evaluation. The following numbers do not follow the same endodontic treatment over time, but individual treatments in each category. Patients were placed into each category based on amount of follow-up time, and success percentages were calculated out of the number of patients followed-up in that time frame.* **RC therapy** - 7 extracted (6 for non-endodontic reasons, 1 periapical complications) - 1 to 6 months (n = 52): 75% - >6 to 24 months (n = 64): 88% - 2-year (12% of original sample size (646), n = 77): 90% success **Pulpotomy** - 1 to 6 months (n = 19): 95%	*pulpotomy could be an alternative to root canal treatment in vital permanent teeth in patients with anatomical difficulties for catheterisation." Page 1161*

Table 4b: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
- >6 to 24 months (n = 13): 100% - 2-year (n = 0): 0% success	

CEM= calcium-enriched mixture; GA = general anesthetic; LTF = lost to follow-up; MTA = mineral trioxide aggregate; PAI = periapical index; PG = pulpotomy group; PP = partial pulpotomy; PPI = preoperative periapical involvement; pre-op = pre-operation/ive; RC = root canal; RCT= randomized controlled trial; SD = standard deviation; TP = total pulpotomy; VAS = visual analogue scale; VPT= vital pulp therapy; ZOE = zinc oxide and eugenol.

Table 4c: Summary of Findings of Included Economic Evaluation

Main Study Findings	Authors' Conclusion
Schwendicke, 2014[11]	
<u>*Base case Results*</u> - Base case: €–516.11 /retention years <u>*Subgroup and Sensitivity Analysis*</u> - Age 50 years: €–78.25/retention years ○ DPC was less expensive and more effective than RC in older patients (> 40 years) or in teeth with a proximal instead of an occlusal exposure site. - Anterior Tooth: €97.46/retention years ○ No treatment was dominant in anterior teeth - 1% Annual Discount Rate: €–180.73/retention years - 5% Annual Discount Rate: €–743.12/retention years ○ Discount rate did not change cost-effectiveness ranking but affected DPC costs more strongly than RC therapy - Only teeth causing pain: €111.23/retention years ○ If teeth causing pain after DPC did not always receive RC but the teeth were extracted in 10% of the cases, DPC would be less effective but still less costly than RC therapy *Mean time until follow-up treatment required* DPC = 17 years RC = 44 years *P* = significant	*"DPC generated significantly lower costs than RC… leading to RC… being dominated by DPC. DPC was not always the more effective option, but it was never the more costly option." Page 1767* *"Although the probability of DPC being the more cost-effective option decreased with increasing willingness to pay ceiling values, it remained more cost-effective irrespective of the chosen ceiling value." Page 1768* *"…the present study found both DPC and RC… suitable to treat pulpal exposures occurring during caries removal in teeth with initially sensible, nonsymptomatic pulps. Based on our estimates, DPC is especially cost-effective for treating pulpal exposure in younger patients, posterior teeth, and occlusal sites but might be less effective and more costly than RC… in older patients, anterior teeth, and proximal exposure sites. The probability and the type of follow-up treatments influence the long-term cost-effectiveness of the initial therapies." Page 1769*

DPC = direct pulp capping trial; RC = root canal.

Appendix 5: Additional References of Potential Interest

Bioceramic materials for pulp capping or partial pulpotomy: clinical effectiveness and safety. (*CADTH Rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2017. https://www.cadth.ca/bioceramic-materials-pulp-capping-or-partial-pulpotomy-clinical-effectiveness-and-safety

Anderson JA. Vital pulp therapy for adult patients with deep carious lesions is a viable short-term alternative to root canal therapy. (*Critically appraised topic*). San Antonio (TX): The University of Texas Health Science Center at San Antonio. 2017: https://cats.uthscsa.edu/found_cats_view.php?id=3280&vSearch=

Garcia O. Coronal pulpotomy can be an effective alternative to conventional root canal treatment. (*Critically appraised topic*). San Antonio (TX): The University of Texas Health Science Center at San Antonio. 2016: https://cats.uthscsa.edu/found_cats_view.php?id=3044&vSearch=